Biomarkers for Health Consequences

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Reducing Tobacco Harm Conference

Biomarkers of Health Consequences
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1. Why do we need biomarkers?

   - Most tobacco-related diseases take years to develop
   - For most health effects, it is impossible to explicitly test the safety of harm reduction interventions in a reasonably short period of time

2. Categories of exposure and biomarkers

   - External exposure markers
   - Biomarkers of exposure (internal dose)
   - Biologically effective dose
   - Biomarkers of potential harm

3. Biomarkers of exposure

   - Nicotine
   - Cotinine
   - Anabasine, anatabine
   - Carbon monoxide
   - Thiocyanate

- Tobacco-specific nitrosamines (NNAL)
- Polycyclic hydrocarbons (1-hydroxypyrene)
- 4-aminobiphenyl
- Urine mutagenicity

4. Biologically effective dose

- Carboxyhemoglobin
- Lipid peroxidation product – F_2-isoprostane
- Carcinogen-DNA adducts:

  PAH, 4-aminobiphenyl, NNK, 8-hydroxydeoxyguanosine
- Carcinogen-hemoglobin adducts:

  PAH, 4-aminobiphenyl

5. Biomarkers of potential harm: biochemical

- Cardiovascular

  Lipids, platelet aggregation (TxB_2 metabolites)
- Inflammatory markers (WBC, C-reactive protein, fibrinogen)
- Lipid peroxidation markers
- Blood viscosity, red cell mass
- Cancer

  Chromosomal alterations

Mutations in non-diseased tissue

Premalignant changes

Hypermethylation of genes

- Lung disease

  Bronchoalveolar lavage (inflammatory cells, cytokines, alpha 1-antitrypsin activity)

6. Biomarkers of potential harm: pathophysiological

- Cardiovascular

  Heart rate and blood pressure

  Arrhythmia monitoring

  Exercise testing

  Cardiac nuclear perfusion studies

- Lung disease

  Pulmonary function tests

- Body weight

7. Direct assessment of harm: some smoking-related diseases that might be assessed in a relatively short period of time

- Pregnancy outcome – birth weight of newborn
- Acute cardiovascular events
- Periodontal disease

- Osteoporosis (bone density)

8. Key gaps in knowledge or behavior

- Importance of single tobacco smoke constituents vs. mixtures of toxins
- Exposure (dose) – response data are inadequate
- Biomarkers need to be validated, both in relation to exposure and as predictors of disease risk
- New biomarkers are needed that reflect pathophysiology, impact of long-term exposure and reversibility of disease risk
- Sources of individual variation and risk (genetic, ethnicity, gender and others) need to be better understood

8. Top research questions

(1.)How can external exposure data best be used to predict internal exposure and disease risk? This includes studies of individual tobacco constituents vs. mixtures, studies of dose-response.

(2.)How can internal exposure measurements best be used to predict smoking-related disease risk?

(3.)Develop novel biomarkers of disease that better reflect pathophysiology and better predict disease risk, including reversibility of disease risk.

(4.)Develop genetic and other markers of individual susceptibility to tobacco-related disease that could be used in combination with information on exposure and biomarker data to better predict the risk for individuals and vulnerable populations.

(5.)Need to develop strategies to study changing disease risk for smoking-related diseases that might become manifest or improve in relatively short periods of time.